

in 2005-2010. The etiology and type of valvular heart disease have been classified on the basis of surgical reports.

**Results:** The distribution of etiologies differed significantly different between the two periods ( $p<0.0001$ ). We noted a decrease in rheumatic valvular disease with 1,558 cases (95%) in the first period and 894 cases (81%) in the second period. Consistently, we observed an increase in degenerative etiology from 1.6% to 16%, and particularly fibroelastic degeneration: 20 (1.6%) and 146 (13.3%) cases. The mechanism of valvular disease (mitral regurgitation versus mixed mitral valve disease and mitral stenosis) differed significantly ( $p<0.0001$ ) for both periods. With regard to mitral regurgitation cases only, degenerative etiologies increased from 11.4% to 38.5% of cases between the two periods ( $p<0.0001$ ). Patients had a mean age of 36.3 years with a female predominance (two thirds of patients), especially in rheumatic etiologies. Age ( $p<0.0001$ ) and the proportion of urban residents ( $p=0.04$ ) was increased in degenerative causes.

**Conclusion:** The study shows the emergence of degenerative valvular disease in Vietnam and a decrease in rheumatic valvular heart disease, which nevertheless remains the most common etiology.

## 0493

### Mutations in the gene encoding FilGAP as a cause for mitral valve prolapse

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The mitral valve prolapse (MVP) is a common cardiac disorder which affects 2-4% of the population and remains one of the most frequent indications for valvular surgery. The familial nature of MVP has been proposed for many years and so far, *FLNA* remains the only identified gene.

Recently, it has been shown that *FLNA* mutations deregulate the RhoA/Rac1 GTPases balance and provided evidences for a role of the Rac1 specific GTPase activating protein, FilGAP, in this network. FilGAP is a recognized FlnA-binding RhoGTPase-activating protein.

Giving the tight interactions of FlnA and FilGAP, we first tested, using a candidate gene approach, the hypothesis that FilGAP, encoded by *ARHGAP24*, could be involved in MVP.

We have sequenced *ARHGAP24* in 95 MVP operated patients and identified 3 rare missense mutations in highly conserve residues (FilGAP p.R95Q; p.P417H and p.T481M). One mutation was novel and the 2 others present a minor allele frequency lower than 0.1% in EVS. Moreover, p.T481M co-segregates with the pathology in a family with 3 affected patients.

We then investigated the impact of these mutations in HEK293 cells. The role of FilGAP is to decrease Rac1 activity and thus to regulate cell processes involved in actin cytoskeleton properties as adhesion, protrusion and intracellular dynamics.

From pull-down assays, we have shown that FilGAP mutations alter Rac1 GTPase activity and significantly decrease the FilGAP interaction with the active form of Rac1 ( $p<0.01$ ). We have also shown, using the XCELLigence system, that cell adhesion and spreading was significantly increased with mutated FilGAP ( $p<0.01$ ). Our results indicate that *ARHGAP24* variants are loss-function mutations.

Moreover, we demonstrate that FilGAP mutations alter the downstream signaling pathway by two different mechanisms. FilGAP p.P417H and p.T481M decrease the interaction with FlnA while p.R95Q impacts the plasma membrane anchorage.

This work reinforces the involvement of GTPases pathway in MVP pathogenesis.

## 0539

### Value of the mean mitral gradient predictive of dyspnea in mitral stenosis in stress echo Doppler cardiac at peak effort

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**Background:** In stress echo Doppler cardiac of mitral stenosis (MS), the cut point of the mean mitral gradient (MMG) at the peak of the effort proposed by the American Recommendations for mitral dilation is 15mmHg. However, this value is questioned in the literature

**Objective:** In stress echo Doppler, determine the peak effort cutoff value of the MMG prediction of the occurrence of dyspnea justifying percutaneous mitral dilation in patients with MS

**Methodology:** Prospective descriptive study conducted in the Cardiology Department Hospital Beni Messous (Algiers) between March 2008 and December 2010. Have been included patients with mitral area  $\leq 2$  cm<sup>2</sup>, functional class I to III NYHA and systolic pulmonary artery pressure  $\leq 60$ mm Hg at rest. Dyspnea was sought to stress test on a treadmill (30W/3min). Dyspneic patients are those who have stopped the examination for a load  $\leq 90$ W due to the occurrence of severe dyspnea. The stress echo Doppler was performed on table echocardiography (30W/3min). The MMG was measured at baseline and at the end of each level to the peak of the effort

**Results:** Three hundred patients were included (mean age  $42.3 \pm 1.3$  years, 81.3% female). At the end of the stress test, 182 had dyspnea (60.6%). Areas under the curve of the MMG at peak stress is equal to 0.80, 95% confidence interval = 0.75-0.85 ( $p<10^{-3}$ ). In predicting dyspnea justifying percutaneous mitral dilation, the optimal cutoff value of the MMG corresponds to 33.5 mmHg: sensitivity=0.55, specificity=0.96, positive likelihood=13.21, positive predictive value (PPV) =95%, positive predictive error (PPE) =5%, Informative Expected Capacity (IEC) =109. However, the diagnostic quality of the MMG at maximum effort with the cut point of 15 mmHg proposed by the American Recommendations is low: sensitivity=0.98, specificity=0.008, positive likelihood=0.98, PPV=60.0%, PPE=40.0%, IEC= 0.25.

**Conclusion:** In this study, the optimal cutoff value of the MMG predictive peak effort dyspnea justifying the percutaneous mitral dilation is 33.5 mmHg, above the cut point proposed by American Guidelines.

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## 0179

### Assessment of paravalvular aortic regurgitation after transcatheter aortic valve implantation using cardiac magnetic resonance imaging: a comparative study with echocardiography and angiography

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Assessment of paravalvular aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI) using Edwards SAPIEN XT valve remains challenging using transthoracic echocardiography (TTE) or angiography. Cardiac magnetic resonance imaging (c-MRI) has a low intraobserver and interobserver variability in the assessment of regurgitant volumes and might be more reliable to assess AR post-TAVI. We therefore aimed to evaluate the value of c-MRI to assess paravalvular AR after TAVI. Between February 2012 and March 2013, 132 consecutive patients underwent successful TAVI using exclusively Edwards SAPIEN XT prosthesis. AR was evaluated by c-MRI, TTE and angiography in 45 patients (27 women, mean age  $84.1 \pm 7.1$  years). Angiography was performed immediately after TAVI whereas TTE and c-MRI were performed one month after implantation. At baseline c-MRI, the mean aortic regurgitant fraction (ARF) was  $21.3 \pm 12.5\%$ . A significant AR ( $\geq$  grade II) was present in 24 (56%) patients using c-MRI ( $30 < \text{ARF} \leq 50\%$ ) whereas it was only observed in 18 (40%) and 12 (27%) patients using TTE and angiography, respectively. Interestingly, there was a poor correlation between c-MRI and TTE ( $r=0.16$ ,  $p=0.28$ ) and between c-MRI and angiography ( $r=0.30$ ,  $p=0.06$ ). In contrast, there was a good correlation between TTE and angiography ( $r=0.6$ ,  $p<0.001$ ). TTE underestimated AR by one degree in 9 patients, and by two degrees in 6 patients as compared to c-MRI. The results of our study suggest that TTE and angiography may underestimate